PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing
(day/month/year) 9 June 2005 (09.06.2005)

Applicant's or agent's file reference
PCT 306

REPLY DUE
within 1 months/~~days~~ from
the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/KR 2003/000665	3 April 2003 (03.04.2003)	

International Patent Classification (IPC) or both national classification and IPC
IPC[7]: C12N 15/87

Applicant
KOREA ADVANCED INSTITUTE OF SCIENCE AND TECHNOLOGY

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:
   - I. ☒ Basis of the opinion
   - II. ☐ Priority
   - III. ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV. ☐ Lack of unity of invention
   - V. ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI. ☐ Certain documents cited
   - VII. ☐ Certain defects in the international application
   - VIII. ☐ Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

   When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

   How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

   Also For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4bis. For an informal communication with the examiner, see Rule 66.6.

   If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 03.08.2005.

Name and mailing address of the IPEA/AT
Austrian Patent Office
Dresdner Straße 87, A-1200 Vienna

Facsimile No. 1/53424/200

Authorized officer
MOSSER R.

Telephone No. 1/53424/437

Form PCT/IPEA/408 (cover sheet) (July 1998)

WRITTEN OPINION

International application No.
PCT/KR 2003/000665

I. Basis of the opinion

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:
pages , as originally filed
pages , filed with the demand
pages , filed with the letter of .

☐ the claims:
pages , as originally filed
pages , as amended (together with any statement) under Article 19
pages , filed with the demand
pages , filed with the letter of .

☐ the drawings:
pages , as originally filed
pages , filed with the demand
pages , filed with the letter of .

☐ the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , filed with the letter of .

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages .

☐ the claims, Nos. .

☐ the drawings, sheets/fig .

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as „originally filed".*

WRITTEN OPINION

International application No.
PCT/KR 2003/000665

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	8, 11-14	YES
	Claims	1-7, 9, 10	NO
Inventive step (IS)	Claims	8, 11-14	YES
	Claims	1-7, 9, 10	NO
Industrial applicability (IA)	Claims	1-14	YES
	Claims	----	NO

Citations and explanations

The following documents have been cited in the Search Report:

D1: US6221959B1
D2: WO2000/040742A1
D3: WO1998/059064A1
D4: WO2002/043769A2
D5: US5714166A

D1 concerns compositions for stabilizing polynucleic acids and increasing the ability of polynucleic acids to cross cell membranes and act in the interior of a cell. In one aspect, D1 provides a polynucleotide complex between a polynucleotide and certain polyether block copolymers. The polynucleotide complex can further include a polycationic polymer, as well as suitable targeting molecules and surfactants. D1 also provides a polynucleotide complex between a polynucleotide and a block copolymer comprising a polyether block and a polycation block.
These polycationic and other polymers are more or less hydrophilic and they have usually high molecular weights, e.g. from 500 to 50.000 or more. Thus, the subject-matters of claims 1-3 are not novel. Also many water-soluble polymers, such as polyvinylpyrrolidones and polyoxazolines are mentioned in D1 (column 10, lines 65-67). Therefore, claim 4 is not new. D1 pertains rather to non-covalent polynucleotide/polymer complex (see claim 1 of D1). But also covalent binding is taken in consideration (column 1, lines 10-12). Present claim 5 concerns covalent binding. That means also claim 5 is not novel. Claim 6 also concerns covalent binding – also this claim is not new. For claim 7 is clear that typical oligos such as antisense oligonucleotides or RNA must be transferred into cells. Antisense oligos etc. are subject-matter of D1 as well. Consequently novelty is not recognized for the subject-matter of claim 7. The biodegradability of the polymers of D1 is not so clear. However, the polymers are not toxic and they will probably be degraded earlier or later. Therefore, no inventive step can be seen in the subject-matter of claim 9. The coupling compounds of claim 10 are well known. For example carbonyldiimidazole is used according to D1 which means that claim 10 is not new.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Box V (page 1)

Claim 8 relates to special oncogenes which are not obvious from D1. Also KALA of claim 12 is not obvious from D1. Claim 11 and the following claims concerning complex micelles are also not obvious. It is difficult for a person skilled in the art to predict which micelle can or will be obtained with different compounds. Thus, novelty and inventive step are recognized for the subject-matters of the claims 8 and 11-14.

D2 pertains to a cellular transport system for the transfer of a nucleic acid through the nuclear envelope. The nuclear transport agent has a module which specifically binds covalently to the terminal sequence of the DNA molecule. Said module comprises a synthetic peptide, a protein, a peptide nucleic acid, or a recombinant protein that specifically binds to the DNA molecule. Such proteins and peptide nucleic acids are also hydrophilic polymers with high molecular weights. Therefore, D2 destroys novelty of claims which concern non organic-chemistry polymers (= proteins etc.). These are the claims 1-3, 5, 9, and 10. There is no doubt that a protein is biodegradable. Consequently, claim 9 is not new.
The other claims are not anticipated by D2.

D3 deals with complexes of nucleic acid and polyethyleneimine (PEI), wherein PEI is modified with a hydrophilic polymer covalently coupled thereto. Claim 1 is not anticipated or obvious from D3. Thus, also the dependent claims 2-14 are not obvious from D3.

D4 concerns stable colloid containing an aqueous phase having suspended therein DNA. This is obviously not the subject-matter of present claims.

D5 concerns star polymers. From this document the subject-matter of the claims 1-14 are not obvious either.

Industrial applicability is obvious for the subject-matters of all claims.